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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,247	BAR-OR, DAVID	
	Examiner	Art Unit	
	Samuel W. Liu	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-66,72-77,81 and 186-280* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 54-61,63-66,73,75-77,200-209,211-215,229-238,240,242-244,255-264,266 and 268-270.

Continuation of Disposition of Claims: Claims rejected are 46-53,62,72,74,81,186-199,210,216-228,239,241,245-254,265,267,271-273 and 275-280.

DETAILED ACTION

Status of the claims

Claims 46-66, 72-77, 81 and 186-280 are pending.

The amendment filed 11/15/06, which adds claims 186-280, amends claims 46 and 57 and cancels claims 1-45, 67-71, 78-80 and 82-185 has been entered. Application request (filed 11/15/06) for extension of time of three months has been entered.

Priority

Applicant's claim for the benefit of a prior-filed application 60429924 filed 11/27/2002 under 35 U.S.C. 119(e) is acknowledged. However, 60429924 dose not have full support for claims 49 (limitation "chicken phosvitin"), 50-53 and 275-280 (limitation "% dephosphorylation"), claims 186-199, 210, 216-228, 239, 241, 245-254, 265, 267 and 271 (limitation "not an aqueous solution or a lyophilized material"), and claims 272-273 (limitation "target molecule attached to"). Thus, these claims are granted priority only to the instant filing date 11/25/03.

Election/Restrictions

At page 20, the response filed 11/15/06 submits that applicant continues to traverse this requirement for an additional election. The response submits that the phosphate acceptor compounds (PACs, IPACs, or EPACs), and submits that said compounds have common features, e.g., useful in treating disease (intended use) mediated by increased phosphorylation of proteins or peptides by kinase. The applicants' arguments are found unpersuasive because intended use "useful in ...") has no patentable weight, and thus, it is not the common structural feature for

said compounds. It is of note that the restriction requirement has been made FINAL (see the Office action mailed 5/15/06). Applicant is directed to said Office action.

Because applicant has elected the phosvitin for examination, any claims drawn to the composition comprising polypeptide which is NOT the phosvitin are withdrawn from further consideration; these claims are: claims 54-61, 63-66, 73, 75-77, 200-209, 211-215, 229-238, 240, 242-244, 255-264, 266, and 268-270. New claims 271-273 and 275-280 are drawn into the elected invention. Thus, claims 46-53, 62, 72, 74, 81, 186-199, 210, 216-228, 239, 241, 245-254, 265, 267, 271-280 are examined in this Office action.

IDS

The references cited in the IDS filed 7/6/06 have been considered by Examiner.

Withdrawal of objections/rejections of claims and the specification

- The rejection to claim 80 is now withdrawn in light of cancellation f the claim; and objection of the specification is withdrawn in light of the amendment to the specification thereof.

- The rejection of claims 67 and 81 under 35 USC, 112 second paragraph is now withdrawn in light of cancellation of claim 67 and the applicant's augment regarding claim 81 is persuasive.

- The rejections of (i) claims 46-49, 62, 67-70, 72, 74, 79 and 185 by Istituto Farmacologico Serono [**IFS**]; (ii) claims 46-49, 62, 67-70, 72, 74, 79 and 185 a by Caprino L.; (iii) claims 46-53, 62, 72, 74 and 79-80 by Jiang et al.; and (iv) claim 81 by Pierce under 35 USC 102 are now withdrawn in light of the amendment to the claims thereof.

• The rejections of claims 46-47, 49, 62, 71-72, 74 and 79 by Mckay under 35 USC 103(a) is now withdrawn in light of the amendment/cancellation of the claims thereof.

New-Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46-53, 62, 72, 74, 186-199, 210, 216-228, 239, 241, 245-254, 265, 267, 271 and 280 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide support for the invention as now claimed.

This is a New Matter rejection for the following reasons:

The amended claim 46 and new claim 186 and dependent claims thereto recite the new limitation "pharmaceutical composition ... is not an aqueous solution or lyophilized material"; the limitation represents a departure from the specification and the claims as originally filed.

At [0088], the specification sets forth that the "formulations may be in the form of a suspension in an aqueous or non-aqueous liquid", which appears to describe that the suspension is non-aqueous but lacks adequate/clear description for that the formulation is NOT aqueous.

At [0107], the specification sets forth that the pharmaceutical compositions "comprise one or more compounds in combination with one or more pharmaceutically-acceptable sterile isotonic aqueous or non-aqueous solutions". Here, combination of the "compounds" with "non-

aqueous solution" within the pharmaceutical composition cannot substitute for the description of the limitation "the pharmaceutical composition is NOT an aqueous".

In addition, at [0108], the specification sets forth "suitable aqueous and nonaqueous carriers". This is not considered to be an adequate description for the limitation "the pharmaceutical composition is NOT an aqueous" either.

At [0112], the specification sets forth that the formulations may be stored in a lyophilized form; however, nowhere in the specification describes that the pharmaceutical composition/formulation is NOT the lyophilized material.

Based the above discussions, therefore, the specification lacks adequate written description for the above-mentioned limitation. The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Claim Rejections - 35 USC § 112, the second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 76, 247-254 and 272-279 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 76 remains rejected because the claim is unclear in whether or not the recited "*a random sequence*" refers to any combination of amino acids derived from the PAC

polypeptide/peptide or any fragments or subsequences thereof. The specification does not define what the *random sequence* is.

Claim 247 (new) recites the limitation "the composition of claim 210 wherein the PAC is ... EPAC". Becasue the limitation of claim 210 from which claim 247 depends is solely directed to "the PAC is ... IPAC", there is insufficient antecedent basis for this limitation in claim 210. Claims 248-254 depending from claim 247 are also rejected.

Claim 272 (new) recites "attached to"; the recitation is unclear whether or not it refers to an association via non-covalent bond or/and linkage via covalent bond. The specification at [0167] and [0204] sets forth that "EPACs adhered to, adsorbed onto, bound to, attached to..."; it appears that "*attached to*" lacks clear metes and bounds; does it refers to "adhered to", "adsorbed onto" or/and "bound to" thereof? The specification does not provide clear definition or meaning thereof. Claims 273-279 which depend from claim 272 are also rejected because these claims do not cure the defect of claim 272.

The applicant's response to the rejection under 35 USC 112, second paragraph

At page 22, the response filed 11/15/06 argues that claim 76 is not indefinite because the specification has defined it at page 12, lines 5-18. The applicant's argument is found unpersuasive because at said page the specification does not define "random sequence" but rather mention "random peptide libraries" (page 12, line 14).

New-Duplicate Claims –Warning

Applicant is advised that should claims 265 and 210 be found allowable, claims 265 and 210 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the

same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- *New*- Claims 46-49, 62, 72, 74, 186, 192-194, 210, 217, 220-223, 239, 241, 246-249, 265 and 267 are rejected under 35 U.S.C. 102(b) as being anticipated by Wuelknitz et al. (US Pat. No. 5279814).

In the patent claims 1-2, Wuelknitz et al. teach a dental composition comprising phosvitin which is inherently partially dephosphorylated (see "*Discussion of art*" [1]) wherein said dental composition is in form of a toothpaste or a gel (patent claim 2), which anticipates instant claims 46 and 186.

Since the phosvitin can act as either an extracellular phosphate acceptor compound (EPAC), or intracellular phosphate acceptor compound (IPAC), the above teaching anticipates instant claims 47-48, 72, 192-193, 210, 221-222, 239, 247-248 and 265.

The phosvitin obtained from SIGMA (col. 5, line 47) which is prepared from chicken egg yolk (see "*Discussion of art*" [2]). This anticipates instant claims 49, 194, 223 and 249.

Being a kinase substrate is the inherent property of the phosvitin (see "*Discussion of art*" [1]), the above teachings anticipate instant claim 62, 74, 241 and 267.

The Wuelknitz et al. composition is applicable for mouthwash which is considered to be a topical administration route, which anticipates instant claim 217.

The composition is formulated as a gel (patent claim 2), which anticipates instant claim 220.

The composition is formulated as a tooth cream (col. 1, line 57), which anticipates instant claim 246.

- *New*- Claims 46-49, 62, 72, 74, 186, 192-194, 210, 210, 216-217, 219, 221-223, 239, 241, 245, 247-249, 265, 267 and 271-274 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakamura et al. (*J. Agric. Food Chem.* (1998) 46, 3958-3963).

Nakamura et al. teach a composition comprising phosvitin conjugated with galactomannan (i.e., phosvitin-galactomannan conjugate) in a powder form (see page 3959, left column, lines 1-10, and Figure 1), wherein the powder sample is not considered to be a lyophilized material because said powder sample is obtained from incubation the phosvitin (freeze-dried) with galactomannan under humidity of 65%, which anticipate claims 186, 216 and 219.

Because, like unconjugated phosvitin, the phosvitin-galactomannan conjugate can also act as phosphate acceptor compound (PAC), the above Nakamura et al. teachings anticipate claim 46.

The phosvitin acts as either extracellular phosphate acceptor compound (EPAC) or intracellular phosphate acceptor compound (IPAC), which anticipates claims 47-48, 72, 192-193, 210, 210, 221-222, 239, 247-248, 265 and 273-274.

In the above phosvitin- galactomannan conjugate, galactomannan is considered to be a targeting molecule wherein the polysaccharide chain (see Figure 5) of galactomannan would target the conjugate to be recognized by an antibody or a receptor or assisting with configuration of phosphoseryl residues of the phosvitin to chelate irons (see page 3960, right column, last seven lines), which anticipates claim 216, 245, and 271-272.

The phosvitin-galactomannan conjugate has improved macromolecular antioxidant activity (see page 3958, right column, 3rd paragraph, page 3962, lines 1-2 form the bottom, and Table 1), suggesting that said conjugate is useful for topical administration for skin due to the improved antioxidant property (antioxidant is formulated in skim composition, e.g., skin cream, see "*Discussion of art*" [5]). This anticipates claim 217.

The phosvitin is prepared from hen egg yolk (see page 3958, right column, last line), which anticipates claims 49, 194, 223 and 249.

Being a kinase substrate is the inherent property of the phosvitin (see "*Discussion of art*" [1]), the above teachings anticipate claims 62, 74, 241 and 267.

• Claim 81 remains rejected under 35 U.S.C. 102(b) as being anticipated by Pierce (*Instructions for GelCode Phosphoprotein staining kit* (2001, March) pages 1-3).

Pierce teaches a kit comprising an EPAC molecule, e.g., phosvitin, wherein reagents of the kit comprising said molecule is packed in separated vials (containers), e.g., "*each phosphoprotein control vial*" (see page 2, line 3). This anticipates instant claim 81.

Note that the claim 81 recitation "*for contacting a cell...*" is considered to be an intended use which has no patentable weight for the claimed kit composition.

The applicant's response to the 102 rejection above

At page 26, the response filed 11/15/06 argues that Pierce kit comprising the container holding the phosvitin which is the positive control wherein the phosvitin has not been dephosphorylated. Thus, the response infers that the rejection should be withdrawn. The applicant's argument is found unpersuasive because the claim as written does not set forth limitation of "dephosphorylation", and because the phosvitin is a biochemical component of the Pierce Kit, its action as "positive control" does not affect its patentable weight since instant kit as written does not exclude said action of the phosvitin. The phosvitin is partially dephosphorylated (see "*Discussion of art*" [1]).

New-Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 46-49, 62, 72, 74, 186, 192-194, 210, 217-218, 220-223, 239, 241, 246-249, 265 and 267 under 35 U.S.C. 103(a) as being unpatentable over Wuelknitz et al. (US Pat. No. 5279814) in view of Shuch et al. (6503483).

The rejection of 46-49, 62, 72, 74, 186, 192-194, 210, 217, 220-223, 239, 241, 246-249, 265 and 267 by Wuelknitz et al. has been discussed above.

Wuelknitz et al. do not expressly teach that the composition is formulated as drops (claim 218).

Wuelknitz et al. teach the dental formulation (col. 1, lines 55-58).

Shuch et al. teach a dental formulation comprising the active component in drops form (see patent claim 19) for oral administration, as applied to claim 218.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate said composition as drops because drops refer to small quantity of the formulation. It would have been within ordinary knowledge and skillfulness of artisan to choose suitable formulation for a particular administration purpose, e.g., formulation as drops taught by Shuch et al. for oral administration. Therefore, it was thus *prima facie* obvious to make and use the dental composition formulated in a special form, e.g., drops.

The applicant's response to the rejection under 35 USC 102

At pages 23-26, the response filed 11/15/06 submits that the naturally-occurring phosvitin is not dephosphorylated, and asserts that the kinase is able to phosphorylate the phosvitin due to the presence of phosphatase activity which dephosphorylates the phosvitin. Hence, applicant requests withdrawal of the 102 rejections. The applicant's argument is found unpersuasive because in fact the phosvitin is not fully phosphorylated. Support for this has been provided by the factual indicia from Platt et al. (*Eur. J. Biochem.* (1988) 176, 61-67). Platt et al. teach that phosvitin is specifically phosphorylated by *M. gallisepticum* protein kinase, as shown by that ^{32}P was incorporated to a large extent into phosvitin (see page 65, left column, 2nd paragraph), wherein the phosphorylation reaction is performed under condition without phosphatase activity

since the reaction is carried out in the presence of the phosphatase inhibitor NaF (see abstract and page 62, left column, 3rd paragraph, lines 1-3). This eliminates possibility of reversible dephosphorylation and phosphorylation.

Conclusion

No claims are allowed.

Discussion of the art

The prior art made of record and not currently relied upon in any rejections is considered pertinent to Applicants' disclosure:

(1) Platt et al. (*Eur. J. Biochem.* (1988) 176, 61-67) teach that phosvitin is specifically phosphorylated by *M. gallisepticum* protein kinase, i.e., phosvitin is partially dephosphorylated as shown by ^{32}P was incorporated to a large extent into phosvitin (see page 65, left column, 2nd paragraph). The phosphorylation is performed in the absence of phosphatase activity because the phosphorylation reaction is carried out in a solution containing the phosphatase inhibitor NaF (see abstract and page 62, left column, 3rd paragraph, lines 1-3).

(2) SIGMA (P1253 Phosvitin from egg yolk (2007, updated) http://www.sigmaaldrich.com/catalog/search/ProductDetail/SIGMA/P1253?PrtPrv=1, page 1) teach that the product phosvitin is prepared from chicken egg yolk.

(3) Khan et al. (*J. Agric. Food Chem.* (1998) 46, 4977-4981) teach emulsion formulation comprising phosvitin (see Table 1). However, this formulation is not a pharmaceutical composition because final emulsion preparation contains SDS detergent (see page 4978, left column, 7th paragraph). Thus, this reference is not a prior art.

(4) Aluko et al. (*J. Agric. Food Chem.* (1997) 45, 4564-4570) teach emulsion formulation comprising phosvitin (see Table 1). However, this formulation is not a pharmaceutical composition because the solution used for emulsifying the phosvitin comprises imidazole, acetate and borate buffer which are not pharmaceutically compatible; and thus, said formulation is not the pharmaceutical composition. Therefore, this reference is disqualified as the prior art.

(5) Mausner J. (US Pat. No. 5922331) teach a skin cream composition comprising the antioxidant component (see patent claim 24).

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon, can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval IPAIRI system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAG only. For more information about the PAN system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SWL

Samuel Wei Liu, Ph.D.
Art Unit 1656, Examiner
May 10, 2006

ROBERT A. WAX
PRIMARY EXAMINER